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Article in *Dermatologic Surgery* · March 2019

DOI: 10.1097/DSS.0000000000001894

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# Platelet-Rich Plasma as a Treatment for Androgenetic Alopecia

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**BACKGROUND** Platelet-rich plasma (PRP) treatment may encourage hair growth by promoting cellular maturation, differentiation, and proliferation.

**OBJECTIVE** The objective of this study was to evaluate the effectiveness of PRP as a treatment for androgenetic alopecia (AGA).

**MATERIALS AND METHODS** A literature search combined with meta-analysis was used to calculate the overall standardized mean difference (SMD) in hair density in patients treated with PRP injections in comparison with baseline and placebo treatment. Chi squared analysis and Fisher exact test were used to investigate variation in protocols.

**RESULTS** The overall SMD in hair density was 0.58 (95% confidence interval [CI]: 0.35–0.80) and 0.51 (95% CI: 0.23–0.80,  $p < .0004$ ) in favor of PRP treatment when compared with baseline and placebo treatment, respectively.

**CONCLUSION** Platelet-rich plasma is beneficial in the treatment of AGA. It is recommended that 3 monthly sessions of PRP (once monthly  $\times$ 3 treatments) be used followed by a 3- to 6-month maintenance period.

*The authors have indicated no significant interest with commercial supporters.*

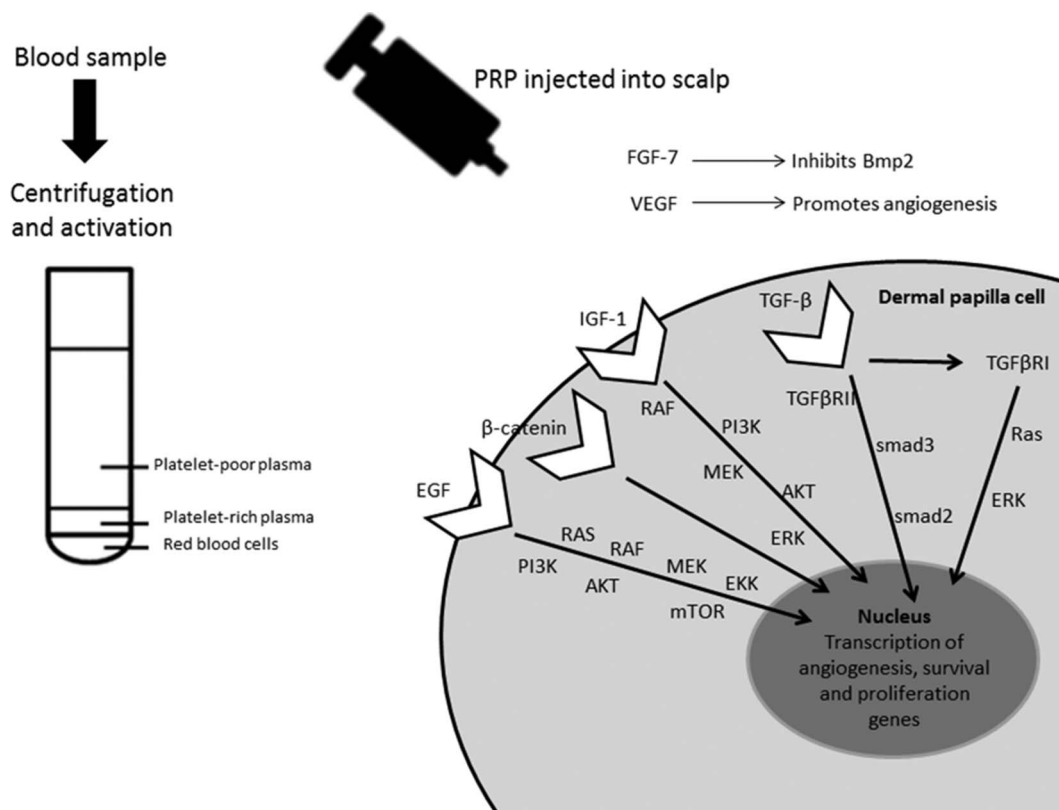
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Platelet-rich plasma (PRP) is created through concentrating platelets found in whole blood.<sup>1</sup> It can aid in tissue regeneration, bone regeneration, and wound repair.<sup>2–7</sup> Platelet-rich plasma treatment has also been suggested to promote hair growth, encourage cell survival and proliferation, and prolong the anagen phase of the hair cycle.<sup>8–13</sup> Platelet-rich plasma is thought to exert its effects in androgenetic alopecia (AGA) via delivery of

concentrated growth factors to the hair follicle and surrounding area (Figure 1). Emerging evidence has begun to characterize the dermal and follicular response to several growth factors (e.g., platelet-derived growth factor, transforming growth factor beta).<sup>14–17</sup> The main objective of this article was to assess the effectiveness of PRP as a monotherapy and adjunct treatment for male AGA.

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ISSN: 1076-0512 • Dermatol Surg 2019;00:1–12 • DOI: 10.1097/DSS.0000000000001894



**Figure 1.** Mechanism of action. Platelet-rich plasma is prepared from an autologous blood sample that is subsequently centrifuged to concentrate platelets. Platelet-rich plasma is then activated, often with the addition of calcium chloride to stimulate the release of growth factors. Platelet-rich plasma is subsequently injected into the patient's scalp, where various growth factors are thought to stimulate gene upregulation associated with angiogenesis, cell survival, and proliferation. AKT, protein kinase B; EGF, epidermal growth factor; ERK, extracellular signal-regulated kinase; FGF-7, fibroblast growth factor 7; IGF-1, insulin-like growth factor 1; mTOR, mechanistic target of rapamycin; PI3K, phosphoinositide 3-kinase; TGF- $\beta$ , transforming growth factor beta; TGF $\beta$ RI, abrogated transforming growth factor beta receptor I; TGF $\beta$ RII, abrogated transforming growth factor beta receptor II; VEGF, vascular endothelial growth factor; smad2, mothers against decapentaplegic homolog 2; smad3, mothers against decapentaplegic homolog 3.

### Platelet-Rich Plasma as a Monotherapy for Male Androgenetic Alopecia

To analyze the effectiveness of PRP for the treatment of AGA, a meta-analysis was undertaken. A literature search was conducted using PubMed on September 7, 2017 and updated on May 18, 2018. The following terms were used; "PRP," "hair," "platelet-rich plasma," "hair transplant," "hair loss," "androgenetic alopecia," and "alopecia." Studies were included if they evaluated the success of PRP for treatment of AGA using hair density (hairs/cm<sup>2</sup>).<sup>18–27</sup> Studies were excluded if they did not use direct injection, contained less than 5 participants per treatment, included only female participants, patients used alternative treatments (5 $\alpha$ -reductase inhibitors, minoxidil) within

6 months of study start or if insufficient data were provided. Study parameters are listed in Table 1 with characteristics such as a larger patient population and use of controls, comparators, randomization, and blinding generally considered more scientifically rigorous. The meta-analysis was conducted using RevMan 5.3 (Copenhagen, Denmark). Effect size was measured through use of the standardized mean difference (SMD), where treatment versus comparator results close to 0 suggest no difference and increasingly higher scores are associated with improvement. Heterogeneity was evaluated using the  $I^2$  statistic.<sup>28,29</sup> The reported efficacy was compared to baseline measures, and a  $p$ -value < .05 was considered significant. The SMD in hair density was 0.58 (95% confidence interval [CI]: 0.35–0.80) in favor of PRP treatment (10

**TABLE 1. Characteristics of Trials Used in Meta-analysis**

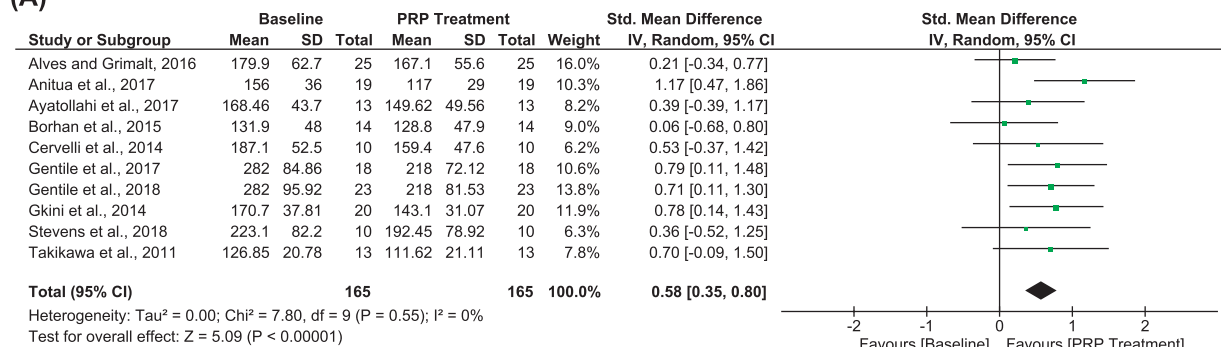
<i>Study</i>	<i>No. of Participants</i>	<i>Placebo or Untreated Control</i>	<i>Use of Comparator</i>	<i>Randomized</i>	<i>Blinded</i>	<i>Length of Study</i>	<i>Study Description</i>
Alves and Gimalt <sup>18</sup>	25	Placebo	No	Yes	Double	6 mo	Half-head study
Anitua and colleagues <sup>19</sup>	19	No	No	No	No	1 yr	Pilot study
Ayatollahi and colleagues <sup>20</sup>	15	No	No	No	No	22 wk	
Borhan and colleagues <sup>21</sup>	17	No	No	No	No	16 wk	Open monocentric and prospective study
Cervelli and colleagues <sup>22</sup>	10	Placebo	No	No	No	12 mo	Half-head study
Gentile and colleagues <sup>23</sup>	18	Placebo	No	Yes	Double	5 mo	Half-head study
Gentile and colleagues <sup>24</sup>	23	Placebo	No	No	No	5 mo	Half-head study
Gkini and colleagues <sup>25</sup>	20	No	No	No	No	1 yr	Prospective cohort study
Stevens and colleagues <sup>26</sup>	10	Untreated	No	No	No	12 wk	
Takikawa and colleagues <sup>27</sup>	26	Placebo	PRP containing dalteparin and protamine particles	No	No	12 wk	
PRP, platelet-rich plasma.							

studies, pooled  $N = 165$ ,  $p < .00001$ ) (Figure 2A). This result is consistent with a previously published meta-analysis that also favored PRP over baseline (SMD: 0.51, 95% CI: 0.14–0.88,  $p = .006$ ).<sup>30</sup> Likewise, PRP exhibited a greater efficacy over placebo treatments (SMD: 0.51, 95% CI: 0.23–0.80,  $p < .0004$ ) with the inclusion of 6 trials (pooled  $N = 99$ )<sup>18,22–24,26,27</sup> (Figure 2B).

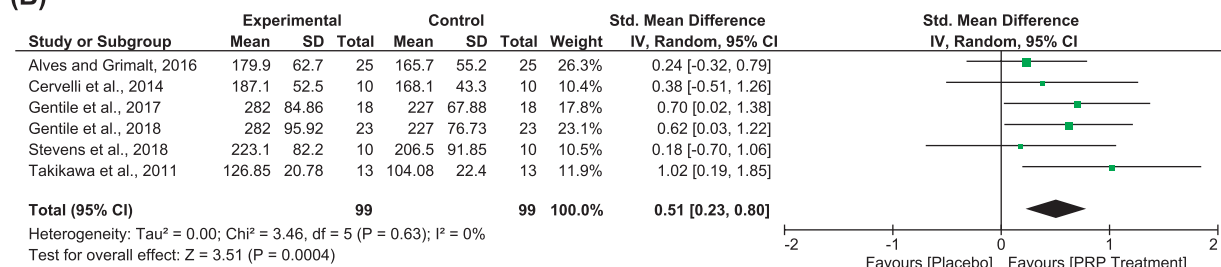
In this study, interestingly, and similar to some of the observations from previous research,<sup>31</sup> evidence for investigating male and female patients separately was found. Inclusion of an all-female study<sup>32</sup> in the current meta-analysis (otherwise composed of all male and mostly male studies) was not possible due to an introduction of high heterogeneity (measured  $I^2 = 89\%$ ), leading to the suggestion that female patients should be investigated distinctly. This idea has practical implications for clinicians as there are few AGA treatment options for female patients and encourages new research directions to test this hypothesis with the possibility of creating a unique PRP protocol targeted directly to female patients.

Investigating methods across AGA studies, with the exception of a few minor modifications, only 2 PRP protocols were duplicated.<sup>33,34</sup> Both studies reported that subjects treated with PRP had a greater change in hair density compared to placebo-treated subjects. Khatu and colleagues and Singhal and colleagues both used an activated (calcium chloride) PRP treatment (2-week interval between sessions, 4 sessions total) created using a double spin technique (1,500 rpm for 6 minutes and 2,500 rpm for 15 minutes).<sup>33,34</sup> These 2 studies did differ in how much PRP was injected; 2 to 3 mL per injection versus 8 to 12 mL per injection.<sup>33,34</sup> Cervelli and colleagues and Gentile and colleagues also used a similar protocol, administering PRP (0.1 mL/cm<sup>2</sup> per injection) every 4 weeks for a total of 3 sessions.<sup>22,35</sup> Both studies used the Cascade-Selphyl-Esforax system, centrifuging the PRP solution at 1,100g for 10 minutes.<sup>22,35</sup> Cervelli and colleagues and Gentile and colleagues reported that PRP-treated patients had a significantly greater mean change in hair density as compared to placebo-treated patients (both studies  $p < .0001$ ).<sup>22,35</sup> Overall, the results suggest that PRP therapy resulted in a significantly greater increase

### (A)



### (B)



**Figure 2.** Forest plot illustrating the results of a meta-analysis of PRP as a treatment for hair loss in AGA patients. (A) Ten studies (pooled  $N = 165$  participants) that used hair density as a measure of efficacy were compared to baseline. (B) Six studies (pooled  $N = 99$  participants) that used hair density as a measure of efficacy were compared to placebo. AGA, androgenetic alopecia; PRP, platelet-rich plasma.

**TABLE 2. Analysis of Platelet-Rich Plasma Protocols and Techniques**

Collection systems	<p>Use of a closed system is recommended for patient safety and reproducibility<sup>24</sup></p> <p>Examples of collection systems that are FDA approved (510k clearance) include the Arthex Angel System,<sup>41</sup> Biomet GPS III,<sup>42</sup> Eclipse PRP system,<sup>43</sup> Emcyte PurePRP Genesis CS concentrating device,<sup>44</sup> Harvest SmartPrep,<sup>45</sup> Magellan TruPRP™,<sup>46</sup> RegenKit Blood Cell Therapy,<sup>47</sup> and the Selphyl system<sup>48</sup></p> <p>Each system incorporates its own feature such as an agar plug that may facilitate a high-volume PRP yield in the Eclipse PRP system,<sup>49</sup> the compartmentalized reservoir bag that enables different mediums (whole blood or mixture of blood and bone marrow) to be separated through centrifugation in the Arthex Angel System,<sup>50</sup> and the use of calcium chloride in the Selphyl System to enhance delivery of growth factors through fibrin matrices created by the conversion of fibrinogen to fibrin<sup>51</sup></p> <p>Each collection system also varies in growth factor and cytokine concentrations, platelet capture efficiencies, and resulting monocyte populations<sup>23,38,39</sup></p> <p>A high platelet recovery rate, elevated growth factor and cytokine concentrations, and a low red blood cell count is desired</p> <p>The optimum platelet concentration has been shown to be 1.5 million per microliter (about 5-fold more concentrated than the normal range of 150,000–400,000),<sup>52</sup> although currently there are no in vivo studies that compare results for hair growth directly</p>
Centrifugation and sonication	<p>During centrifugation, high speeds and long durations can inadvertently precipitate platelets or discharge growth factors (e.g., platelet-derived growth factor), influencing the efficacy of PRP<sup>53,54</sup></p> <p>As a potential alternative to centrifugation, acoustic-based particle manipulation methods could be used to separate blood cells<sup>55</sup></p> <p>Sonication can lyse platelet cell membranes, allowing the release of growth factors and be more effective in separation of red and white blood cells<sup>56</sup></p> <p>Ultrasound-generated PRP demonstrated a greater platelet recovery rate as compared to PRP obtained through centrifugation (<math>79 \pm 9\%</math> vs <math>54 \pm 10\%</math> over baseline, respectively)<sup>56</sup></p> <p>Sonication may increase the survival rate of transplanted follicular units<sup>57</sup></p>
Activation	<p>Activation using calcium chloride or calcium gluconate is frequently used in hair loss studies to induce <math>\alpha</math> granule release of growth factors from platelets<sup>18,23,25,32–34,58–61</sup></p> <p>Extracellular matrix materials such as ACell (FDA approved to repair and remodel damaged tissue) could also be used to activate PRP solutions, although current evidence for this technique remains anecdotal</p> <p>Alternatively, microparticles could be a functional and cheaper substitute<sup>62,63</sup></p> <p>The combination of microparticles, adipose derived stem cells, and follicular stem cells could also be advantageous and are currently under investigation</p> <p>Scalp needling to induce inflammation leading to platelet activation has been suggested to be as effective as use of an exogenous activator<sup>64</sup></p> <p>Similarly, it has been suggested that exogenous activation may not make a significant impact on specific growth factors and cytokines, such as platelet-derived growth factor BB and transforming growth factor <math>\beta 1</math>,<sup>23</sup> although a direct comparison (<math>n = 40</math>) of nonactivated versus calcium chloride-activated PRP resulted in significantly more effective treatment in the former<sup>40</sup></p> <p>Thus, although it is clear that activation is necessary for growth factor release, further research is necessary to determine the impact of various methods of activation on the efficacy of PRP</p>
Needle size	<p>It is unknown if needle size can influence the efficacy of PRP</p> <p>In AGA studies, needles used to administer PRP have ranged from 20 to 32 G, with 30-G needle as the most commonly used<sup>18,19,21,23–26,35,59,64</sup></p>
Injection depth	<p>Follicles vary in length below the skin surface, averaging 4.2 mm in length<sup>65</sup></p> <p>Subdermal injections have been shown to be efficacious and tolerable in a blinded randomized clinical trial (<math>n = 40</math>)<sup>66</sup>; success has been found with intradermal injections, injections into recipient slits during transplantation, and injections into microneedling channels<sup>54,67</sup></p> <p>Use of a mechanical and thus reproducible device has also been recommended for controlled delivery of PRP<sup>24</sup></p>

**TABLE 2. (Continued)**

Treatment frequency and no. of sessions	<p>Monthly PRP injections had a significantly greater increase in hair count as compared to injections every 3 mo (mean percent change of 29.6 vs 7.2%, <math>p &lt; .001</math>)<sup>68</sup></p> <p>Substantial improvements in hair restoration parameters (e.g., hair density, hair count) have frequently been reported in PRP studies that administer 3 monthly sessions, suggesting that 3 sessions may be necessary to achieve desired results<sup>18,22–24,35,60,61</sup></p> <p>A 3- to 6-mo maintenance interval after a monthly PRP treatment regimen could be beneficial<sup>69</sup></p> <p>Follow-up periods should extend to 12 mo post-treatment, as an early decrease in hair density coinciding with the PRP-driven stimulation of hairs into the anagen stage is expected</p>
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AGA, androgenetic alopecia; FDA, Food and Drug Administration; PRP, platelet-rich plasma.

in hair density compared to baseline counts and placebo.

There are a number of factors that could explain the variation seen in PRP results (Table 2). Differences in preparations and delivery have been suggested as a possible explanation.<sup>36,37</sup> In addition to platelet concentration, white blood cell, neutrophil, and red blood cell concentration varies with separation systems as well.<sup>38,39</sup> The resulting effect on efficacy is unknown; however, individual advantages are expected with the various systems.<sup>38</sup> For example, in direct comparison ( $n = 6$ ), the Arthex Angel System resulted in signifi-

cantly improved hair density versus the Regen Cell Therapy collection system.<sup>23</sup>

Patient characteristics may also influence the results of PRP treatment (Table 3). Variables from each study (Table 4) were examined using a chi squared analysis and Fisher exact test to identify any protocol trends that led to significant results more often than expected. Specifically, each variable (population demographics, centrifuge process, concentration of platelets, injection process, needle gauge, method of platelet activation, quantity and intervals of treatment, and time of analysis) was examined in search

**TABLE 3. Factors That Could Influence the Efficacy of Platelet-Rich Plasma**

<i>Patient Characteristics</i>	<i>Evidence</i>
Gender	<p>Male patients experienced new growth 2 wk earlier and had a higher increase in hair counts in comparison to the female population (<math>n = 115</math>)<sup>31</sup></p> <p>Statistically significant increase in the mean total hair density for male patients in comparison to female patients (<math>n = 25</math>)<sup>18</sup></p>
Severity of alopecia	Significantly better response from patients with a lower grade of alopecia (Grade III–IV alopecia, Hamilton–Norwood) <sup>21,25,53,59,70</sup>
Disease duration	<p>Most studies observed a significantly better response from patients with a shorter disease duration<sup>21,53,59</sup></p> <p>Alves and Grimalt<sup>18</sup> observed a statistically significant increase in the mean total hair density in patients with greater than 10 years of disease duration</p>
Age	<p>Alves and Grimalt<sup>18</sup> observed a statistically significant increase in the mean total hair density for patients younger than 40 years</p> <p>Borhan and colleagues<sup>21</sup> observed the best response in patients in their early 30s</p>
Onset of alopecia	Alves and Grimalt <sup>18</sup> observed a statistically significant increase in the mean total hair density for patients with hair loss beginning after 25 years
Presence of vellus hair	Presence of vellus hair led to better results compared to those who had few but normal hair <sup>25,70</sup>



**TABLE 4. Characteristics of Platelet-Rich Plasma Studies Conducted in Androgenetic Alopecia Patients Using Hair Density as a Measure of Efficacy**

Study	Study Type	PRP Method	Concentration Increase	Injection Depth	Needle Gauge	Activation	Treatment Duration	Assessment Date	Results
Kachhawa and colleagues <sup>70</sup>	Split head study of placebo versus PRP, 50 male patients, HN III–VI	Double spin		Intradermal			6 treatments at 21-d intervals	4 mo	Density increased significantly compared to baseline and placebo
Starace and colleagues <sup>71</sup>	Pilot study, open-label, single-group, single-centre study; 10 female patients not responding to treatments; Ludwig I–III	My Cells system			25		Every 2 wks for 4 sessions	12 and 24 wks	Mostly all positive and increasing over time, corresponding to a clinical improvement
Ayatollahi and colleagues <sup>20</sup>	13 male patients, HN III–VI uncontrolled	Regen Lab PRP Kit—RegenACR	Estimate 1.6-fold from Regen Lab data				5 treatments every 2 wks	22 wks	Not significant, $p = .37$
Stevens and colleagues <sup>26</sup>	10 male patients, HN II–III	PRP and adipose-derived stromal vascular fraction, Arthrex Angel System			20		1	6 and 12 wks	Hair density was significantly increased after 6 and 12 wks, $p = .013$ , $p < .013$
Gupta and colleagues <sup>53</sup>	Open-label pilot study, 30 male patients, HN III–VII	Double spin		Massage into scalp		Microneedling	6 treatments at 15-d intervals	6 mo	Increase in hair density is observed but significance is not reported
Gentile and colleagues <sup>23</sup> (study 1)	Half-head comparison with placebo, 18 male patients, HN II–IV	CPunT preparation system	5-fold	5 mm	30		3 treatments at 30-d intervals	12 wks	Significant improvement compared to baseline and placebo as well as to a previous study $p = .0029$
Gentile and colleagues <sup>23</sup> (study 2)	Half-head comparison with comparator, 6 male patients, HN IIIA–IIIV	Regen Blood Cell Therapy or Arthrex Angel System	5-fold		25	Calcium	1 treatment	6 mo	Significant improvement in Arthrex Angel versus Regen Blood Cell Therapy



TABLE 4. (Continued)

Study	Study Type	PRP Method	Concentration Increase	Injection Depth	Needle Gauge	Activation	Treatment Duration	Assessment Date	Results
Alves and Grimalt <sup>18</sup>	Randomized, placebo-controlled, double-blind, half-head parallel-group study; 12 male patients, HN II–V; 13 female patients, Ludwig I–III	Single spin, leukocyte poor	3-fold		30	Calcium	3 treatments at 1-mo intervals	3 and 6 mo	Significant improvement from baseline and placebo $p < .05$
Anitua and colleagues <sup>19</sup>	Uncontrolled study; 13 male patients, HN III–VI; 6 female patients, Ludwig II/frontal	Single spin BTI system, leukocyte layer not collected	2-fold		30		4 treatments at 1-mo intervals with a final treatment at 7 mo	12 mo	Significant improvement $p < .05$
Tawfik and Osman <sup>32</sup>	Double-blinded, randomized, placebo-controlled, half-head study; 30 female patients; Ludwig I–III	Double spin				Calcium	4 treatments at 1-wk intervals	7 mo	Significant improvement $p < .05$ compared to placebo and baseline
Cervelli and colleagues <sup>22</sup>	Randomized, placebo, half-head study; 10 male patients	Cascade-Selphyl-Esforax, 0.1 mL/cm <sup>2</sup> per injection, leukocytes not excluded			30	Calcium	3 treatments at 1-mo intervals	12 mo	Significant improvement, control versus treatment, $p < .0001$
Gkini and colleagues <sup>25</sup>	Prospective cohort study; 18 male patients, HN II–V; 2 female patients; Ludwig I–III	RegenKit BCT-3	5.8-fold	1.5–2.5 mm	27	Calcium	3 treatments at 21-d intervals, booster at 6 mo	12 mo	Significant improvement at 6 wks and 12 mo compared to baseline
Borhan and colleagues <sup>21</sup>	Open, monocentric prospective study, 3 female and 11 male patients, HN III–IV	Regen Lab, 4–5 mL used per session, 0.05–0.1 mL per injection		Superficial dermis	32		4 treatments total at 3-wk intervals, last treatment at 6-wk interval	16 wk	Not significant, $p = .8638$

TABLE 4. (Continued)

Study	Study Type	PRP Method	Concentration Increase	Injection Depth	Needle Gauge	Activation	Treatment Duration	Assessment Date	Results
Gentile and colleagues <sup>35</sup>	Randomized, placebo-controlled, half-head study; 2 male patients; HN II–IV	Modified versions of the Cascade-Selphyl-Esforax system and platelet-rich lipotransfert system, may include leukocytes			30	Calcium	3 treatments at 30-d intervals	2 yrs	Significant improvement in control versus treatment, $p = .001$
Gentile and colleagues <sup>24</sup>	18 male patients, HN I–V; and 5 female patients, Ludwig I–II			5 mm with medical injector gun	30		3 treatments at 30-d intervals	5 mo	$31 \pm 2\%$ increase in hair density for the treatment group versus less than 1% increase in hair density for the placebo group compared to baseline
Takikawa and colleagues, <sup>27</sup>	Controlled, half-head study; 26 participants	Cascade-Selphyl-Esforaxsystem, PRP mixed with 2 mg/mL of D/P MP	6-fold	Subcutaneous injection	25	Calcium	5 treatments at 2-wk intervals; last treatment at 3-wk intervals	12 wks	No significant difference between PRP and PRP & (D/P MP) treatments but significant improvement from control
D/P MP, dalteparin and protamine microparticles; PRP, platelet-rich plasma.									

**TABLE 5. Recommended Techniques for Platelet-Rich Plasma Treatment of Androgenetic Alopecia**

Treatment frequency and no. of sessions	Three sessions of PRP at 1-mo intervals followed by a 3- to 6-mo maintenance period
Injection depth	Subdermal
Collection systems	Capable of high platelet recovery rate (1.5 million platelets per microliter, <sup>52</sup> which is 5 times basal concentration), although the average reported concentration is 3 times the basal amount and influence of the balance of white blood cells, neutrophils, and red blood cells is still under investigation <sup>38</sup> (Kushida and colleagues, 2014)
Activation	Activation should be considered; however, the best method is up for debate as use of exogenous agents such as calcium chloride have been contrasted with alternate techniques, such as scalp needling, <sup>67</sup> or natural contact with dermal fibroblasts through the PRP preparation and injection process <sup>72</sup>
Centrifugation and sonication	Use of sonication and microparticles is preferred
Needle size	Impact is unclear

PRP, platelet-rich plasma.

of a similar variable appearing more often than by random probability in the protocols of studies which achieved statistically significant results. The use of an exogenous activator appeared the most connected to achieving desirable results ( $p = .08$ ) that was similar to the conclusions of an earlier meta-analysis.<sup>30</sup>

Nonetheless, this suggestion contrasts a direct comparison of nonactivated versus calcium chloride-activated treatments ( $n = 40$ ), which concluded the former to be significantly more effective.<sup>40</sup> From this analysis combined with the results of the meta-analysis (above), specific PRP techniques and methods are recommended (Table 5).

## Conclusions

Platelet-rich plasma could be used to improve hair restoration parameters (e.g., hair density) in AGA monotherapy or adjunct therapy. For the former, 3 sessions of PRP at 1-month intervals followed by a maintenance regimen is recommended.

**Acknowledgments** The authors wish to thank S.G. Versteeg and Dr. M.S. Dotzert of Mediprobe Research Inc., as well as Dr. M.A. Cole for assisting in the writing of this manuscript.

## References

- Dhurat R, Sukesh M. Principles and methods of preparation of platelet-rich plasma: a review and author's perspective. *J Cutan Aesthet Surg* 2014;7:189–97.
- Watt-Smith S. Dental and craniofacial applications of platelet-rich plasma. *Br Dent J* 2005;199:799.
- Lin SS, Montemurro NJ, Krell ES. Orthobiologics in foot and ankle surgery. *J Am Acad Orthop Surg* 2016;24:113–22.
- Bhanot S, Alex JC. Current applications of platelet gels in facial plastic surgery. *Facial Plast Surg* 2002;18:27–33.
- Badran Z, Abdallah MN, Torres J, Tamimi F. Platelet concentrates for bone regeneration: current evidence and future challenges. *Platelets* 2017;29:105–112.
- Soffer E, Ouhayoun JP, Dosquet C, Meunier A, et al. Effects of platelet lysates on select bone cell functions. *Clin Oral Implants Res* 2004;15: 581–8.
- Gaviño Orduña JF, Caviedes-Bucheli J, Manzanares Céspedes MC, Berástegui Jimeno E, et al. Use of platelet-rich plasma in endodontic procedures in adults: regeneration or repair? A report of 3 cases with 5 years of follow-up. *J Endod* 2017;43:1294–1301.
- El-Sharkawy H, Kantarci A, Deady J, Hasturk H, et al. Platelet-rich plasma: growth factors and pro- and anti-inflammatory properties. *J Periodontol* 2007;78:661–9.
- Shumez H, Prasad P, Kaviarasan P, Deepika R. Intraleisional platelet rich plasma vs intraleisional triamcinolone IN the treatment OF alopecia areata: a comparative study. *Int J Med Res Health Sci* 2014;4:118–22.
- Gilhar A, Etzioni A, Paus R. Alopecia areata. *N Engl J Med* 2012;366: 1515–25.
- Hudgens JL, Sugg KB, Grekin JA, Gumucio JP, et al. Platelet-rich plasma activates proinflammatory signaling pathways and induces oxidative stress in tendon fibroblasts. *Am J Sports Med* 2016;44:1931–40.
- Gupta AK, Carviel J. A mechanistic model of platelet-rich plasma treatment for androgenetic alopecia. *Dermatol Surg Off Publ Am Soc Dermatol Surg Al* 2016;42:1335–9.
- Li ZJ, Choi HI, Choi DK, Sohn KC, et al. Autologous platelet-rich plasma: a potential therapeutic tool for promoting hair growth. *Dermatol Surg* 2012;38(7 pt 1):1040–6.
- Heldin CH, Westermark B. Mechanism of action and in vivo role of platelet-derived growth factor. *Physiol Rev* 1999;79:1283–316.
- Botchkarev VA, Botchkareva NV, Nakamura M, Huber O, et al. Noggin is required for induction of the hair follicle growth phase in postnatal skin. *FASEB J* 2001;15:2205–14.
- Yano K, Brown LF, Detmar M. Control of hair growth and follicle size by VEGF-mediated angiogenesis. *J Clin Invest* 2001;107: 409–17.

17. Oshimori N, Fuchs E. Paracrine TGF- $\beta$  signaling counterbalances BMP-mediated repression in hair follicle stem cell activation. *Cell Stem Cell* 2012;10:63–75.
18. Alves R, Grimalt R. Randomized placebo-controlled, double-blind, half-head study to assess the efficacy of platelet-rich plasma on the treatment of androgenetic alopecia. *Dermatol Surg Off Publ Am Soc Dermatol Surg Al* 2016;42:491–7.
19. Anitua E, Pino A, Martinez N, Orive G, et al. The effect of plasma rich in growth factors on pattern hair loss: a pilot study. *Dermatol Surg* 2017;43:658–70.
20. Ayatollahi A, Hosseini H, Shahdi M, AhmadNasrollahi S, et al. Platelet-rich plasma by single spin process in male pattern androgenetic alopecia: is it an effective treatment? *Indian Dermatol Online J* 2017;8:460–4.
21. Borhan R, Gasnier C, Reygagne P. Autologous platelet rich plasma as a treatment of male androgenetic alopecia: study of 14 cases. *J Clin Exp Dermatol Res [internet]* 2015. Available from: <http://www.omicsonline.org/open-access/autologous-platelet-rich-plasma-as-a-treatment-of-male-androgenetic-alopecia-study-of-14-cases-2155-9554-10000292.php?aid=57866>. Accessed January 26, 2016.
22. Cervelli V, Garcovich S, Bielli A, Cervelli G, et al. The effect of autologous activated platelet rich plasma (AA-PRP) injection on pattern hair loss: clinical and histomorphometric evaluation. *Biomed Res Int* 2014;2014:760709.
23. Gentile P, Cole JP, Cole MA, Garcovich S, et al. Evaluation of not-activated and activated PRP in hair loss treatment: role of growth factor and cytokine concentrations obtained by different collection systems. *Int J Mol Sci* 2017;18:PMC5343942.
24. Gentile P, Garcovich S, Scioli MG, Bielli A, et al. Mechanical and controlled PRP injections in patients affected by androgenetic alopecia. *J Vis Exp* 2018. doi: 10.3791/56406.
25. Gkini M-A, Kouskousik A-E, Tripsianis G, Rigopoulos D, et al. Study of platelet-rich plasma injections in the treatment of androgenetic alopecia through an one-year period. *J Cutan Aesthet Surg* 2014;7:213–9.
26. Stevens HP, Donners S, de Bruijn J. Introducing platelet-rich stroma: platelet-rich plasma (PRP) and stromal vascular fraction (SVF) combined for the treatment of androgenetic alopecia. *Aesthet Surg J* 2018;38:111–22.
27. Takikawa M, Nakamura S, Nakamura S, Ishirara M, et al. Enhanced effect of platelet-rich plasma containing a new carrier on hair growth. *Dermatol Surg* 2011;37:1721–9.
28. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;21:1539–58.
29. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–60.
30. Gupta AK, Carviel JL. Meta-analysis of efficacy of platelet-rich plasma therapy for androgenetic alopecia. *J Dermatolog Treat* 2017;28:55–8.
31. Garg S, Manchanda S. Platelet-rich plasma-an “Elixir” for treatment of alopecia: personal experience on 117 patients with review of literature. *Stem Cell Investig* 2017;4:64.
32. Tawfik AA, Osman MAR. The effect of autologous activated platelet-rich plasma injection on female pattern hair loss: a randomized placebo-controlled study. *J Cosmet Dermatol* 2018;17:47–53.
33. Khatu SS, More YE, Gokhale NR, Chavhan DC, et al. Platelet-rich plasma in androgenic alopecia: myth or an effective tool. *J Cutan Aesthet Surg* 2014;7:107–10.
34. Singhal P, Agarwal S, Dhoot PS, Sayal SK. Efficacy of platelet-rich plasma in treatment of androgenic alopecia. *Asian J Transfus Sci* 2015;9:159–62.
35. Gentile P, Garcovich S, Bielli A, Scioli MG, et al. The effect of platelet-rich plasma in hair regrowth: a randomized placebo-controlled trial. *Stem Cell Transl Med* 2015;4:1317–23.
36. Castillo TN, Pouliot MA, Kim HJ, Dragoo JL. Comparison of growth factor and platelet concentration from commercial platelet-rich plasma separation systems. *Am J Sports Med* 2011;39:266–71.
37. Mazzocca AD, McCarthy MBR, Chowanec DM, Cote MP, et al. Platelet-rich plasma differs according to preparation method and human variability. *J Bone Joint Surg Am* 2012;94:308–16.
38. Kushida S, Kakudo N, Morimoto N, Hara T, et al. Platelet and growth factor concentrations in activated platelet-rich plasma: a comparison of seven commercial separation systems. *J Artif Organs Off J Jpn Soc Artif Organs* 2014;17:186–92.
39. Degen RM, Bernard JA, Oliver KS, Dines JS. Commercial separation systems designed for preparation of platelet-rich plasma yield differences in cellular composition. *HSS J* 2017;13:75–80.
40. Ince B, Yildirim MEC, Dadaci M, Avunduk MC, et al. Comparison of the efficacy of homologous and autologous platelet-rich plasma (PRP) for treating androgenic alopecia. *Aesthet Plast Surg* 2018;42:297–303.
41. *Angel System [internet]*. Arthrex; 2018. Available from: <https://www.arthrex.com/orthobiologics/arthrex-angel-system/products>. Accessed April 25, 2018.
42. *GPS III Platelet Concentration System [internet]*. Zimmer Biomet; 2018. Available from: <http://www.zimmerbiomet.com/medical-professionals/biologics/product/gps-iii-platelet-concentration-system.html>. Accessed April 25, 2018.
43. *Eclipse PRP [internet]*. 2018. Available from: <http://4d1hkmkgfyq3nu45k2kso51x.wpengine.netdna-cdn.com/wp-content/uploads/2017/06/Eclipse-PRP-Sales-Sheet.compressed.pdf>. Accessed April 25, 2018.
44. *PurePRP® [internet]*. Emcyte Corporation; 2018. Available from: <https://www.emcyte.com/pureprp-sp/pureprp-sp-features.html>. Accessed April 25, 2018.
45. *Platelet-Rich Plasma (PRP) Prepared Using the Harvest® SmartPrep® Multicellular Processing System [internet]*. Harvest TerumoBCT; 2018. Available from: <https://www.harvesttech.com/clinician/clinician-home/prp/products>. Accessed April 25, 2018.
46. *Discover Tru PRP Brochure [internet]*. Discover Tru PRP; 2018. Available from: <http://www.discovertru-prp.com/>. Accessed April 25, 2018.
47. *RegenKit® BCT—A-PRP®—PRP®—RegenPRPTM—Regen Extracell® Product Highlights [internet]*. Regenlab USA PRP & Cell Therapy Specialists; 2018. Available from: <https://www.regenlabusa.com/>. Accessed April 25, 2018.
48. *What Is Platelet-Rich Plasma (PRP)? [internet]*. Selphyl; 2018. Available from: <http://selphyl.com/about-prfm/>. Accessed April 25, 2018.
49. *About Eclipse PRP [internet]*. Eclipse; 2017. Available from: <http://eclipseaesthetics.com/products/eclipse-prpl>. Accessed April 25, 2018.
50. *Angel® Concentrated Platelet Rich Plasma (cPRP) System—Operator's Manual [internet]*. Angel Concentrated Platelet Rich Plasma (cPRP) System; 2018. Available from: [https://d1psc3qesfsa61.cloudfront.net/pdfs/8Lq9CG43TUySLQFBDdSuGw/8Lq9CG43TUySLQFBDdSuGw.pdf?Expires=1524580697&Signature=MzHL0DGRSITeV655ScGR8-tWbmZrEhbifD6wM4RmcKzT20M1cgeNTNhpGABjCqaVDqubpGkv4oPM5cHKW9vE2cGL88zwrDeqd5R51MV5wi~0oTth00mxQYob8NggEYnt43PRI9KuREkD51jXsUeY7ofYr-eJspxxsmzYaJsJhY1lF5zxzk4SCQmJqhZdXNoK9dXGinteBtXjIfHewMif~nYp1vvmrazRv-hCGK7mSVpMRC9xwH5mUeqGXNyyt93H-QdSeUDTydM6lbiK3z9S-8IU1yX~VQ-INyQ~E1Sd69Hg-ybrCL-INcZUuQzpfbhEqqkvpaXD~1beaPKDP~g\\_\\_&Key-Pair-Id=APKAJMGJRW6JXSOBMSLA](https://d1psc3qesfsa61.cloudfront.net/pdfs/8Lq9CG43TUySLQFBDdSuGw/8Lq9CG43TUySLQFBDdSuGw.pdf?Expires=1524580697&Signature=MzHL0DGRSITeV655ScGR8-tWbmZrEhbifD6wM4RmcKzT20M1cgeNTNhpGABjCqaVDqubpGkv4oPM5cHKW9vE2cGL88zwrDeqd5R51MV5wi~0oTth00mxQYob8NggEYnt43PRI9KuREkD51jXsUeY7ofYr-eJspxxsmzYaJsJhY1lF5zxzk4SCQmJqhZdXNoK9dXGinteBtXjIfHewMif~nYp1vvmrazRv-hCGK7mSVpMRC9xwH5mUeqGXNyyt93H-QdSeUDTydM6lbiK3z9S-8IU1yX~VQ-INyQ~E1Sd69Hg-ybrCL-INcZUuQzpfbhEqqkvpaXD~1beaPKDP~g__&Key-Pair-Id=APKAJMGJRW6JXSOBMSLA). Accessed April 25, 2018.

51. Sclafani AP. Applications of platelet-rich fibrin matrix in facial plastic surgery. *Facial Plast Surg FPS* 2009;25:270–6.
52. Giusti I, Rughetti A, D'Ascenzo S, Millimaggi D, et al. Identification of an optimal concentration of platelet gel for promoting angiogenesis in human endothelial cells. *Transfusion (Paris)* 2009;49:771–8.
53. Gupta S, Revathi TN, Sacchidanand S, Nataraj HV. A study of the efficacy of platelet-rich plasma in the treatment of androgenetic alopecia in males. *Indian J Dermatol Venereol Leprol* 2017;83:412.
54. Garg S. Outcome of intra-operative injected platelet-rich plasma therapy during follicular unit extraction hair transplant: a prospective randomised study in forty patients. *J Cutan Aesthet Surg* 2016;9:157–64.
55. Nam J, Lim H, Kim D, Shin S. Separation of platelets from whole blood using standing surface acoustic waves in a microchannel. *Lab Chip* 2011;11:3361–4.
56. Wu Y, Kanna MS, Liu C, Zhou Y, et al. Generation of autologous platelet-rich plasma by the ultrasonic standing waves. *IEEE Trans Biomed Eng* 2016;63:1642–52.
57. Cole J, Cole M, Insalaco C, Cervelli V, et al. Alopecia and platelet-derived therapies. *Stem Cell Investig* 2017;4:1–8.
58. Ferrando J, García-García SC, González-de-Cossío AC, Bou L, et al. A proposal of an effective platelet-rich plasma protocol for the treatment of androgenetic alopecia. *Int J Trichology* 2017;9:165–70.
59. Mapar MA, Shahriari S, Haghighizadeh MH. Efficacy of platelet-rich plasma in the treatment of androgenetic (male-patterned) alopecia: a pilot randomized controlled trial. *J Cosmet Laser Ther Off Publ Eur Soc Laser Dermatol* 2016;18:452–5.
60. El Taieb MA, Ibrahim H, Nada EA, Seif Al-Din M. Platelets rich plasma versus minoxidil 5% in treatment of alopecia areata: a trichoscopic evaluation. *Dermatol Ther* 2017;30. doi: 10.1111/dth.12437.
61. Trink A, Sorbellini E, Bezzola P, Rodella L, et al. A randomized, double-blind, placebo- and active-controlled, half-head study to evaluate the effects of platelet-rich plasma on alopecia areata. *Br J Dermatol* 2013;169:690–4.
62. *Acell, Inc. Receives New FDA Clearances, Prepares for Future Growth [internet]*. ACell; 2015 Available from: <https://acell.com/acell-inc-receives-new-fda-clearances-prepares-for-future-growth/>. Accessed April 24, 2018.
63. *Acell®, Inc. Receives FDA Clearance for Concurrent Use of its Wound Management Devices [internet]*. ACell; 2016. Available from: <https://acell.com/acell-inc-receives-fda-clearance-for-concurrent-use-of-its-wound-management-devices/>. Accessed April 24, 2018.
64. Schiavone G, Raskovic D, Greco J, Abeni D. Platelet-rich plasma for androgenetic alopecia: a pilot study. *Dermatol Surg Off Publ Am Soc Dermatol Surg* 2014;40:1010–9.
65. Jimenez F, Izeta A, Poblet E. Morphometric analysis of the human scalp hair follicle: practical implications for the hair transplant surgeon and hair regeneration studies. *Dermatol Surg Off Publ Am Soc Dermatol Surg* 2011;37:58–64.
66. Hausauer A, Jones D. Evaluating the efficacy of different platelet-rich plasma regimens for management of androgenetic alopecia: a single-center, blinded, randomized clinical trial. *Dermatol Surg* 2018;44:1191–200.
67. Puig CJ, Reese R, Peters M. Double-Blind, placebo-controlled pilot study on the use of platelet-rich plasma in women with female androgenetic alopecia. *Dermatol Surg Off Publ Am Soc Dermatol Surg* 2016;42:1243–7.
68. *Platelet-rich Plasma Injections Efficacious for Androgenetic Alopecia [internet]*. Healio Dermatology; 2017 Available from: <https://www.healio.com/dermatology/hair-nails/news/online/%7B3b5c08ba-9c29-4487-85be-0cf2f00aeac4%7D/platelet-rich-plasma-injections-efficacious-for-androgenetic-alopecia>. Accessed March 27, 2018.
69. Picard F, Hersant B, Niddam J, Meningaud J-P. Injections of platelet-rich plasma for androgenic alopecia: a systematic review. *J Stomatol Oral Maxillofac Surg* 2017;118:291–7.
70. Kachhawa D, Vats G, Sonare D, Rao P, et al. A split head study of efficacy of placebo versus platelet-rich plasma injections in the treatment of androgenic alopecia. *J Cutan Aesthet Surg* 2017;10:86–9.
71. Starace M, Alessandrini A, D'Acunto C, Melandri D, et al. Platelet-rich plasma on female androgenetic alopecia: tested on 10 patients. *J Cosmet Dermatol* 2018;18:59–64.
72. Arshdeep, Kumaran MS. Platelet-rich plasma in dermatology: boon or a bane? *Indian J Dermatol Venereol Leprol* 2014;80:5–14.

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